Zinc supplementation for pediatric pneumonia

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Abstract

Question Among young children suffering from pneumonia, zinc deficiency has been documented in many countries. Is supplementation with zinc effective in the treatment and prevention of childhood pneumonia?

Answer Several studies reported that zinc supplementation for more than 3 months was effective for preventing pneumonia in children younger than 5 years of age; however, the evidence is not sufficient to confirm its prophylactic properties if it is given for shorter periods of time. Adjunctive zinc supplementation for treatment of pneumonia has failed to show a benefit.

L'apport complémentaire en zinc pour la pneumonie chez l'enfant

Résumé

Question Il a été documenté dans de nombreux pays que les jeunes enfants souffrant de pneumonie avaient une carence en zinc. L'apport complémentaire en zinc est-il efficace dans le traitement et la prévention de la pneumonie durant l'enfance?

Réponse Plusieurs études ont signalé que l'apport complémentaire en zinc pendant plus de 3 mois était efficace pour prévenir la pneumonie chez les enfants de moins de 5 ans; toutefois, les données probantes sont insuffisantes pour confirmer ses propriétés prophylactiques s'il est administré sur de plus courtes périodes de temps. Il n'a pas été démontré que l'apport complémentaire en zinc comme traitement d'appoint de la pneumonie apportait des bienfaits.

Pneumonia in children is caused by viral or bacterial pathogens.[1] The incidence of childhood pneumonia is higher in low- and middle-income countries, with 0.22 episodes per child-year[2] compared with an incidence of 0.05 episodes per child-year in high-income countries.[2] Pneumonia was the cause of death for 920 000 children younger than 5 years of age globally in 2015, accounting for 16% of childhood deaths.[1,3] The proportion of deaths from pneumonia is highest among children in South Asia and sub-Saharan Africa.[1,3]

Treatment of pneumonia includes antimicrobial agents, supportive management with oxygen supplementation, intravenous fluids, and antipyretics.[1,4] Immunization, breastfeeding, adequate nutrition, and good sanitation help prevent pneumonia.[5-7]

Zinc is an important micronutrient supporting growth and normal function of the immune system.[8] Zinc deficiency results in growth impairment, anorexia, behavioural changes, and impaired immune function, leading to susceptibility to infections.[9] Unlike Canadian children who have good dietary sources of zinc,[10,11] children in developing countries are at a high risk of deficiency due to inadequate zinc in their diets.[9] Zinc supplementation has been shown to reduce the duration and limit the complications of diarrhea in children by increasing intestinal fluid absorption, supporting mucosal integrity, and enhancing immune response.[10,12]

Therapeutic role of zinc for pneumonia

The use of zinc as adjunctive therapy for pneumonia was evaluated in several countries. Results from a randomized, double-blind, placebo-controlled trial of zinc supplementation (25 mg per day) with antibiotics for radiology-confirmed acute pneumonia in 94 hospitalized children aged 6 to 36 months in Tanzania showed no significant reduction in the duration of hospitalization (incidence rate ratio [IRR] = 0.69; 95% CI 0.45 to 1.06; $P = .09$) or in the proportion of children hospitalized for less than 3 days (risk ratio [RR] = 0.85; 95% CI 0.57 to 1.25; $P = .40$) and less than 5 days (RR = 1.01; 95% CI 0.83 to 1.23; $P = .92$) when compared with placebo.[13] Moreover, no significant differences were observed between groups in the duration of fever, tachypnea, nasal flaring, chest indrawing, or changes of antibiotics. Vomiting within 15 minutes of treatment was also not significantly different between groups. The mean change in plasma zinc concentration per 12 hours of hospitalization was not significantly different between zinc-supplementation and placebo groups.

Among 96 Chinese children aged 1 to 12 months hospitalized owing to severe pneumonia, those with low

serum zinc levels were assigned to treatment or control groups.[14] After treatment, serum zinc levels increased in the treatment group and returned to normal levels on day 12 (SD=2); however, no statistical differences were detected in the mean (SD) length of hospital stay (9.0 [6.0] vs 7.0 [4.0]; *P*=.12) or duration of mechanical ventilation (6.0 [5.0] vs 3.5 [3.0]; *P*=0.13) between groups. Similarly, in a 2011 systematic review of 4 trials with 3200 children aged 2 to 35 months in Bangladesh, Nepal, and India, adjunctive zinc supplementation failed to show a statistically significant effect on clinical recovery from both severe and nonsevere pneumonia (fixed effect RR=1.02; 95% CI 0.93 to 1.11).[15] There were no significant differences in resolution of tachypnea, chest indrawing, or duration of hospital stay for severe pneumonia between zinc and placebo groups. The role of zinc supplementation as an adjunct to antibiotics for severe pneumonia was further examined in a 2016 meta-analysis with 9 randomized controlled studies of 3000 children younger than 5 years of age.[16] Zinc supplementation did not significantly reduce the time to recovery (hazard ratio [HR]=1.04; 95% CI 0.90 to 1.19; *P*=.58), hospital length of stay (HR=1.04; 95% CI 0.83 to 1.33; *P*=.74), treatment failure (RR=0.95; 95% CI 0.79 to 1.14; *P*=.58), or changes of antibiotics (RR=1.07; 95% CI 0.79 to 1.45; *P*=.67) when compared with placebo. No significant differences between groups were observed in death rate, adverse events (vomiting and deterioration), or recovery times for severe pneumonia indicators (tachypnea, hypoxemia, chest indrawing, and fever).

A meta-analysis of 7 randomized controlled trials with 1066 children from developing countries, hospitalized for severe acute lower respiratory tract infection (ALTI, defined as respiratory rate more than 50 breaths per minute with crepitation on auscultation and chest indrawing, with or without hazardous signs), compared the therapeutic role of zinc with placebo.[17] Time of resolution of severe illness (standardized mean difference of -0.15; 95% CI -0.5 to 0.2; *P*=.4) and duration of hospitalization (standardized mean difference of -0.29; 95% CI -0.68 to -0.09; *P*=.13) were not statistically different between groups. Moreover, no significant differences between groups were noted in time to resolution of all parameters (hypoxia, chest indrawing, and tachypnea), change of antibiotics, or treatment failure rates. Adverse events other than vomiting (odds ratio of 0.25; 95% CI 0.20 to 0.30) were not significantly different.

The combined current evidence suggests there is no role for the prescription of zinc as an adjunctive therapy for pediatric pneumonia.

Prophylactic role of zinc supplementation

Several studies have also been exploring the effect of zinc supplementation on prevention of pediatric pneumonia. A meta-analysis published in 2011 included 8 randomized controlled trials in children younger than 5 years of age from developing countries and reported that zinc supplementation alone (10 to 20 mg), for more than 3 months, was associated with a significant reduction in the rate of pneumonia by 19%, with an RR of 0.81 (95% CI 0.73 to 0.90) when compared with the control group (placebo, vitamins, other minerals).[18] Mortality was not statistically different (RR=0.85; 95% CI 0.65 to 1.11). Similar results were reported in a recent meta-analysis of 6 randomized controlled studies involving 5200 children 2 to 59 months of age in Bangladesh, India, Peru, and South Africa.[19] Zinc supplementation for at least 3 months was associated with a 13% reduction in the incidence (fixed-effect RR=0.87; 95% CI 0.81 to 0.94) and a 41% reduction in the prevalence (random-effects RR=0.59; 95% CI 0.35 to 0.99) of pneumonia. However, a randomized controlled trial from Nepal reported conflicting results.[20] Zinc supplementation (10 to 20 mg per day) or placebo was given for 14 days to 2600 children aged 2 to 35 months with community-acquired pneumonia. Despite higher serum zinc levels in the treatment group, the median number of days until the first episode of pneumonia 6 months after initial supplementation was not significantly different between zinc and placebo groups, with HRs of 1.02 (95% CI 0.92 to 1.14) and 1.11 (95% CI 0.72 to 1.73) for nonsevere pneumonia and severe pneumonia, respectively. These findings suggests that short-course zinc supplementation during an infection does not prevent pneumonia during the following 6 months.

A 2010 meta-analysis with 10 randomized controlled trials included results from 50 000 children younger than 5 years of age with ALTI who received either zinc (daily or weekly with a total dose of at least 70 mg per week) or placebo for more than 3 months. Zinc significantly reduced the incidence of ALTI if it was diagnosed by a health care provider based on rapid respiratory rate and at least 1 other sign (chest wall indrawing, nasal flaring, fever, cyanosis, lethargy, or convulsion) with or without abnormal lung sounds.[21] The IRR of the zinc group compared with the placebo group was 0.65 (95% CI 0.52 to 0.82), indicating that zinc supplementation reduced the incidence of ALTI by 35% (95% CI 18% to 48%). Nevertheless, zinc did not significantly reduce the incidence of ALTI if it was reported by caregivers (IRR=1.01; 95% CI 0.91 to 1.12) or diagnosed by health care providers based only on rapid respiratory rate (IRR=0.96; 95% CI 0.86 to 1.08). Similarly, in a randomized controlled trial in India, the incidence of ALTI (defined as cough with difficult or rapid breathing or chest indrawing, reported by the caregiver) in 272 children 6 to 11 months of age who received oral zinc supplementation (20 mg in 5 mL of syrup) for 2 weeks was lower by 62% (95% CI 0.26 to 0.36) compared with placebo.[22]

In summary, zinc supplementation treatment for longer than 3 months in children younger than 5 years of

age was effective in preventing pneumonia. Evidence related to supplementation for less than 3 months' duration is not as strong.

Conclusion

Providing children younger than 5 years of age with zinc supplementation for longer than 3 months has been shown to be effective for preventing pneumonia. Adjunctive zinc supplementation (with antibiotics) for treatment of pneumonia is currently not recommended. Current evidence supports zinc supplementation for prevention in developing countries where the nutritional status of children is suboptimal compared with children in developed countries. Canadian children who are provided with sufficient zinc from their regular diets might not need to receive supplementation.

Competing interests
None declared

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